Single-breath breath-holding estimate of pulmonary blood flow in man: comparison with direct Fick cardiac output

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SUMMARY

1. Resting pulmonary blood flow ($\dot{Q}$), using the uptake of the soluble inert gas Freon-22 and an indirect estimate of lung tissue volume, has been estimated during breath-holding ($\dot{Q}_c$) and compared with direct Fick cardiac output ($\dot{Q}_f$) in 16 patients with various cardiac disorders.

2. The effect of breath-hold time was investigated by comparing $\dot{Q}_c$ estimated using 6 and 10 s of breath-holding in 17 patients. Repeatability was assessed by duplicate measurements of $\dot{Q}_c$ in the patients and in six normal subjects.

3. $\dot{Q}_c$ tended to overestimate $\dot{Q}_f$, the bias and error being 0.09 l/min and 0.59, respectively. The coefficient of repeatability for $\dot{Q}_c$ in the patients was 0.75 l/min and in the normal subjects was 0.66 l/min. For $\dot{Q}_f$ it was 0.72 l/min. There was no significant difference in $\dot{Q}_c$ measured at the two breath-hold times.

4. The technique is simple to perform, and provides a rapid estimate of $\dot{Q}$, monitoring acute and chronic changes in cardiac output in normal subjects and patients with cardiac disease.

Key words: cardiac output, pulmonary circulation, respiration.

Abbreviations: $\dot{Q}$, pulmonary blood flow; $\dot{Q}_c$, pulmonary blood flow measured by the breath-holding method; $\dot{Q}_f$, direct Fick cardiac output; V_A, alveolar volume; V_t, lung tissue volume.

INTRODUCTION

After the early experiments of Krogh & Lindhard [1], several methods of measuring pulmonary blood flow ($\dot{Q}$) have been introduced which have taken advantage of the solubility of biologically inert gases in blood. The breath-holding technique of Cander & Forster [2] used the uptake of nitrous oxide and acetylene during different periods of breath-holding. The gases are removed from the lungs in two distinct phases: an initial rapid fall in gas concentration due to the solution of the test gases in the pulmonary tissue, and a subsequent gradual fall due to removal by the pulmonary capillary blood flow. From the data, it is possible to estimate the lung tissue volume (V_t) and $\dot{Q}$ during breath-holding ($\dot{Q}_c$). Although this technique gives results comparable with invasive methods, it requires two or more estimations of the uptake of the soluble gas, and is therefore not suitable for following acute changes in $\dot{Q}_c$. Rebreathing methods overcome this problem, but many patients find the respiratory gymnastics rather difficult compared with the requirements of the single-breath breath-holding transfer factor technique. Johnson *et al.* [3] suggested that if V_t was assumed, $\dot{Q}_c$ could be estimated from a single breath-hold. A predicted value of V_t may be derived from the alveolar volume (V_A) [4].

The aims of this study were (1) to compare Q estimated by the single-breath technique, using the soluble inert gas Freon-22, with direct Fick cardiac output at rest ($\dot{Q}_f$), (2) to assess the effects of using different breath-holding times and (3) to determine the repeatability of the single-breath method.

METHODS

Subjects

Studies were performed on 33 patients (age range 44–66 years), without overt cardiac failure, undergoing routine left and right heart cardiac catheterization. Fifteen patients had ischaemic heart disease, seven had mitral valve disease, four had aortic valve disease and seven had a combination of disorders. Six normal subjects (age range 24–35 years) were also tested to investigate the repeatability of the breath-holding technique. Local ethical

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committee approval was given for the study, and each subject gave informed consent.

$\dot{Q}_f$

A Cournand catheter was positioned in the pulmonary artery and a 'pigtail' catheter in the descending aorta. The patient breathed room air via a two-way non-return breathing valve (Hans Rudolf, Kansas City, MO, U.S.A.) initially for 5 min to become accustomed to mouthpiece breathing. A further 5 min period of quiet breathing followed, during which expired air was collected in a Douglas bag. Expired volume was recorded using a Wright's respirometer (BOC Medishield). Arterial and mixed venous blood samples were drawn via the catheters during the gas collection period at a rate of 1 ml/min. A further 5 ml of blood was taken to estimate haemoglobin.

The mixed expired air was analysed for the concentration of oxygen and carbon dioxide using a mass spectrometer (VG Gas Analysis) which had been calibrated with gas mixtures analysed to a tolerance of $\pm 1\%$. Oxygen saturations from the blood samples were measured using a reflection oximeter (American Optical). Oxygen consumption was calculated as described by Cotes [5], and cardiac output using the Fick equation [6].

$\dot{Q}_c$

This was measured by the single-breath breath-holding technique used for the carbon monoxide transfer factor [7], using a test gas mixture of 10% argon, 18% oxygen and 4% Freon-22 in nitrogen. Inspired and expired gas samples were analysed for argon and Freon-22 using the mass spectrometer.

Two estimations of $\dot{Q}_c$ were made using a breath-hold time of 10 s. A rest period of 5 min was allowed between each estimate to allow any residual Freon-22 and argon to be washed out of the lungs.

V_t was calculated as 11.5% V_A [4], where V_A was calculated according to McGrath & Thomson [8]. $\dot{Q}_c$ was calculated using the equation:

$$\dot{Q}_c = \frac{V_A \times 760}{\alpha[V_A/(V_A + \alpha V_t)] \times (P_A - P_{H_2O})} \times \ln\left[\left(\frac{V_A}{V_A + \alpha V_t}\right) \times \frac{F_{A,\text{freon(ti)}}}{F_{A,\text{freon(tt)}}}\right] \text{l/min}$$

where α is the Bunsen solubility coefficient for Freon [$\alpha = 0.73$ ml of gas(STPD)/ml of liquid per atmosphere]. P_A and P_{H_2O} are the absolute alveolar pressure and alveolar water vapour partial pressure, respectively, 760 is the standard barometric pressure in mmHg, and $F_{A,\text{freon(ti)}}$ and $F_{A,\text{freon(tt)}}$ are the inspired and final alveolar concentrations of Freon-22, respectively [9].

Comparison of techniques

Sixteen patients were studied on the same day. Cardiac output was measured during the catheter procedure before angiography. Measurements were made after at least 15 min in the supine position, in a quietened room, with the patient being disturbed as little as possible. No premedication was given. $\dot{Q}$ was measured at the same time. To avoid any order effects, estimates of $\dot{Q}_c$ and $\dot{Q}_f$ were made in a random order.

Effect of breath-hold time

In 17 patients three estimates of $\dot{Q}_c$ was made using breath-hold times in the order 10 s, 6 s, 10 s.

Repeatability

The repeatability of both techniques was assessed using the duplicate measurements of $\dot{Q}_c$ from the 33 patients. In a subset of 9/16 patients, duplicate estimates of $\dot{Q}_f$ were made during the catheter procedure. Repeatability was also assessed in six normal subjects. Subjects were seated for 10 min before any measurements, with a 5 min interval between each estimate. Subjects were requested not to eat or drink for at least 1 h before testing.

Statistical analysis

Analysis of the data was performed using the Minitab statistical package [10]. The effects of breath-hold times were assessed using paired *t*-tests. The coefficient of repeatability [11] was calculated as twice the SD of the difference between duplicate measurements.

The two techniques were formally compared using the analytical techniques of Altman & Bland [12, 13].

RESULTS

All patients and normal subjects completed the studies without difficulty. From the cardiac catheter data, the mean pulmonary arteriolar pressure, pulmonary wedge pressure, pulmonary arterial resistance and cardiac frequency were 24.2 mmHg (range 12–48 mmHg), 16.0 mmHg (range 7–38 mmHg), 1.59 mmHg $\text{min}^{-1}\,\text{l}^{-1}$ (range 1.3–5.7 mmHg) and 79 beats/min (range 49–110 beats/min), respectively. No patient appeared to hyperventilate during the Fick procedure. The mean respiratory exchange ratio for the group was 0.83 (range 0.70–1.01).

Effect of breath-hold time

There was no significant difference between the two 10 s breath-hold times and either of the 10 and 6 s breath-hold times for $\dot{Q}_c$. The mean $\dot{Q}_c$ values ($\pm$SEM) for the breath-hold times in the order 10, 6 and 10 s were 6.21 ± 0.37, 6.16 ± 0.27 and 6.28 ± 1.18 l/min, respectively.

Repeatability

The mean difference between duplicate estimates of $\dot{Q}_c$ in the 33 patients using the same breath-hold time was 0.22 (range −0.63 to 1.21) l/min. The coefficients of repeatability for the direct Fick and single-breath tech-

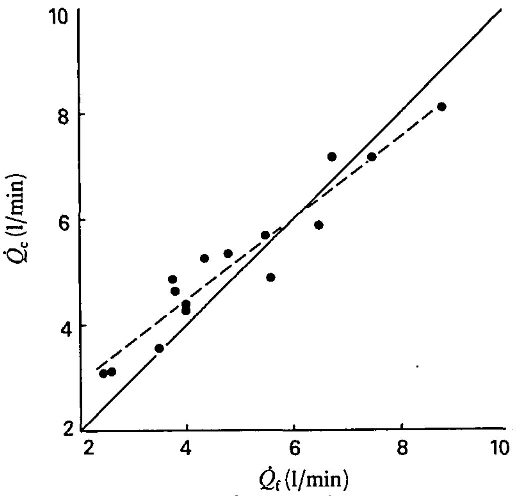

Fig. 1. Comparison of $\dot{Q}_c$ with $\dot{Q}_f$. The solid line is the line of identity, $y = 1.37 + 0.77x \pm 0.49$.

niques were 0.72 l/min and 0.75 l/min, respectively. For the normal subjects, the coefficient of repeatability was 0.66.

Comparison of techniques

The relationship of $\dot{Q}_c$ to $\dot{Q}_f$ for the two groups of data is shown in Fig. 1. Comparison of the data by the method of Altman & Bland [12, 13] revealed that the error (indicated by the SD of the differences) was 0.59 l/min and the bias (indicated by the mean of the difference) was −0.09 l/min towards the $\dot{Q}_c$ measurement. The 95% confidence interval was −0.37 to 0.20 l/min.

DISCUSSION

Cardiac output may be used clinically to monitor therapy and investigate the effects of physiological or chemical stimuli on cardiac function. Accurate measurement of cardiac output with the minimum of physical intervention is desirable, especially if the technique is to have wide application. Cardiac output may either be estimated non-invasively [14], or from estimates of $\dot{Q}$ [1–3, 9], using inert gas uptake. This assumes the absence of a cardiac shunt or serious pulmonary ventilation/perfusion mismatching. If the latter occurs, then measurements of $\dot{Q}$ will represent the blood flow to those areas of the lungs where ventilation and perfusion remain matched, and cardiac output will therefore be underestimated.

In this study the applicability of measuring $\dot{Q}$ using a modification of the Cander & Foster technique [2] was investigated. The technique was well tolerated, taking approximately 15 s to complete the respiratory manoeuvre, and a further 2 min to analyse the gas concentrations.

For very dyspnoeic patients a breath-hold time of less than 10 s would be desirable. Comparison of the 10 and 6 s breath-hold times showed that the use of a 6 s breath-hold time is acceptable. However, in severely ill patients, even a 6 s breath-hold time may be too long.

To be of value the technique must be repeatable. Duplicate estimates in the 33 patients showed a mean difference of 0.22 l/min with a range of −0.63 to 1.21 l/min, the majority of duplicate estimates being quite close.

The comparison of the two techniques showed a tendency towards higher values employing the breath-holding technique. This may be explained by alteration in the cardiac frequency during the breath-holding estimate [15]. During inspiration, venous return and volume to the lungs are increased. On expiration, a decrease in pulmonary blood volume occurs with an increased blood flow to the left side of the heart. Pulmonary venous flow shows a similar variation, but is delayed in time by about one beat. Breath-holding results in a fall in cardiac frequency and a rise in both systolic and diastolic blood pressure. If a Valsalva manoeuvre were to be inadevertently performed during breath-holding, this would cause a reduction in venous return and cardiac output.

The estimation of V_t is important in the calculation of pulmonary blood flow. If V_t had been omitted, $\dot{Q}_c$ would have been overestimated by 12.7–25.3% (mean 15.6%). In patients with pulmonary oedema, V_t would be underestimated. Recalculated $\dot{Q}$ with V_t estimated as 25% V_A showed that $\dot{Q}_c$ would be underestimated by 5.1–16.2% (mean 10.3%). Sera & Yoshitake [16] have shown that V_t, in cardiac disease, does not increase greatly, until the mean pulmonary artery pressure or the pulmonary artery wedge pressure is greatly increased. In this study, although some patients did have high pulmonary artery pressures, all had taken diuretics. Thus, unless $\dot{Q}_c$ is measured in patients with severe pulmonary oedema, the estimation of V_t as 11.5% V_A appears satisfactory.

The single-breath technique investigated in this study is non-invasive, simple to perform, provides a rapid estimate of pulmonary blood flow and is comparable with direct Fick cardiac output. Provided the limitations of soluble inert gas techniques are borne in mind, the technique will provide a good estimate of cardiac output and should be useful in monitoring acute and chronic changes in cardiac output during pharmacological interventions and physiological stimuli [17] at rest. The measurement may be combined with the carbon monoxide transfer factor to provide simultaneous measurements of gas-exchanging capacity and perfusion [18].

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